Protozoa

Introduction

To do protozoa quickly, and a in a high-yield way, we have to strip off a lot of the details that make protozoa difficult. Every organism in this lesson is board relevant. The trouble is that protozoa have their own vocabulary, the medications used to treat them are hard to say, and you won't be exposed to them very much unless you train outside of the United States. That being said, you still must know them for licensure exams. Because they are so difficult, so different, and so few, we placed them at the end of the Microbiology module. If you don't get to them, that's okay. Flashcards are your friend. If you are looking for score augmentation (250+), you must know these lessons cold. If you are looking for average, memorize the tables and snag buzzwords. We try to keep it to must-knows only. This should not be used for a tropical medicine course. We eliminated a lot of the details. You will also notice that very few treatments are listed in bold. While you may be asked to select a treatment, the basic sciences are more about identification of the organism on a slide and understanding the pathogenesis of disease in the human. NOT life cycle of the parasite's sexual reproduction outside the human, but what the parasite does in the human that leads to disease. Treatment is low-yield for the basic sciences in an already low-yield subject.

Protozoa are single-celled organisms. There are two general life cycles you should be aware of. One involves cysts, one does not.

One life cycle involves trophozoites and cysts. These are the intestinal protozoa. The **trophozoite** form is the motile, flagellated, reproducing, and vulnerable form of a protozoan as it exists in the human. The **cyst** form is the nonmotile, nonmetabolizing, nonreproducing form similar to a bacterial spore. Cysts are hardy, difficult to kill, and allow protozoa to exist outside a human for a long time. They are metabolically inactive. When a human eats the cyst, the cyst is exposed to moisture, nutrients, etc., and so the trophozoite excysts in the human. Release of the active cellular form of a bacterial spore was called germination; germination in the protozoan world is "excystment." The thing that comes out of the cyst is the trophozoite. The trophozoite makes more trophozoites, which are then pooped out of the human where they encyst.

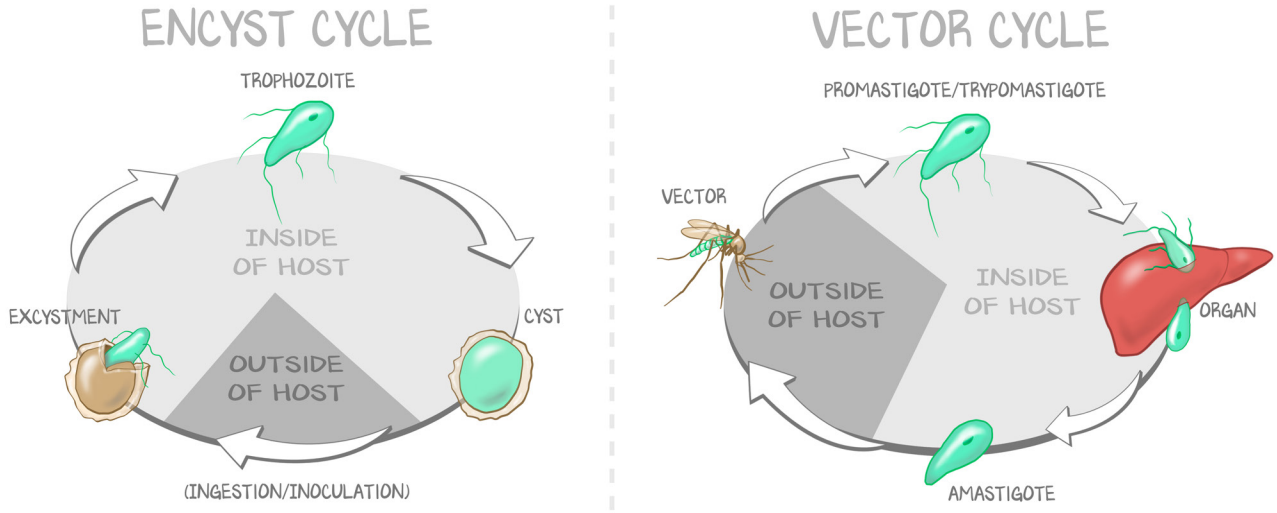


Figure 1.1: Life Cycles of Protozoa
There are several life cycles of protozoa, two of which are relative to the human. In one cycle, the hardy, metabolically inactive cyst form can exist outside of a host. When ingested, the protozoan undergoes excystment, becoming the metabolically active, reproductive, and symptom-inducing adult, known as a trophozoite. In another cycle, the protozoan exists in two forms—flagellated (names vary, depending on the protozoan) and nonflagellated (amastigote). The amastigote is taken up by a vector, outside-the-human magic happens, and the amastigote becomes flagellated. The flagellated form is injected into the human by the vector. The flagellated form swims to its preferred organ (tropism), where it causes symptoms.

One other life cycle doesn't use cysts to live outside humans. Instead, the life cycle involves a flagellated form and a nonflagellated form and is carried by an insect vector. The **flagellated form** (called a promastigote or a trypomastigote) is what is birthed in the vector and injected into the human. The flagellated form gets to the tissue it likes the most, where it becomes the nonflagellated form. The **nonflagellated form** (amastigote) is the form that causes disease in humans, grows in human cells, causing damage to organs. The nonflagellated form is what is birthed in the human and is what the vector sucks up out of the bloodstream.

We've broken up this lesson into categories based on their general life cycle. This table is the outline:

INTESTINAL	UROGENITAL	TISSUE AND BLOOD	OTHER
Entamoeba histolytica	*Trichomonas*	*Trypanosoma cruzi*	*Naegleria fowleri*
Giardia lamblia		*Trypanosoma brucei*	*Toxoplasma gondii*
Cryptosporidium		*Leishmania*	
		Plasmodium species	
		Babesiosis	
Fecal-oral	Sexual	Vector insect	Special

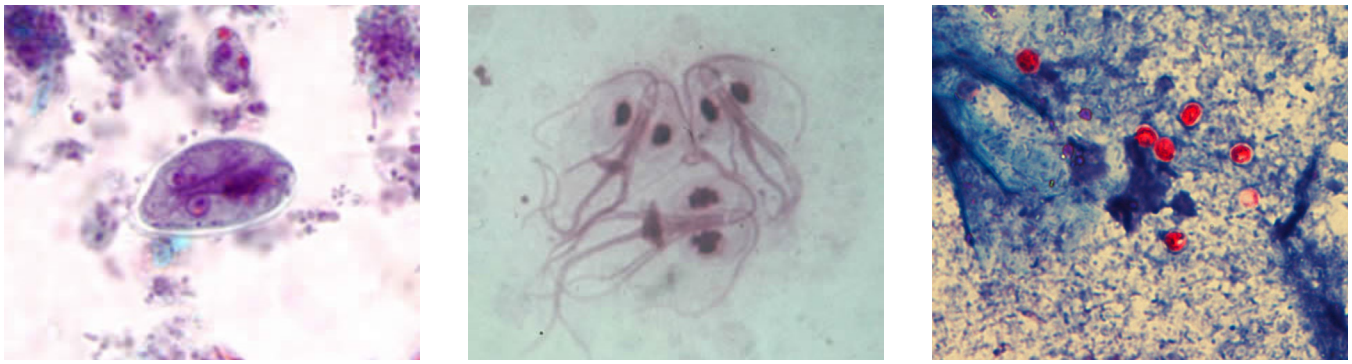
Table 1.1: Types of Protozoa

Intestinal Protozoans

Intestinal protozoa live in the gut. They get ingested through fecal-oral contact. They are ingested as cysts. They become the active protozoa in the gut. They shed cysts into the stool. Cysts live outside humans very well. When ingested, they germinate. Any behavior that increases exposure of the mouth to stool increases the risk of transmission. This shows up in three ways on the exam—contaminated water, daycare centers, and men who have sex with men. Intestinal protozoa are going to present with diarrhea. There are three protozoans you should know about—*Entamoeba histolytica* (bloody diarrhea, liver abscess), *Giardia lamblia* (fatty diarrhea, hiking), and *Cryptosporidium* (watery diarrhea, AIDS).

***Entamoeba histolytica* is bloody diarrhea** and **liver abscess**. *Entamoeba histolytica* is an ameboid protozoan that affects the GI tract, causing a **bloody diarrhea**. It is an invasive organism that burrows into the colonic mucosa. The invasion of the colonic mucosa causes the bloody diarrhea. If a biopsy of the colon is performed, it will show **flask-shaped abscesses** in the mucosa. Because they are invasive to the mucosa, they may penetrate into blood vessels, entering the portal circulation, where they are trapped by the liver, where they become liver abscesses (they are referred to as cysts, but we choose to use abscess to distinguish the microscopic cyst form of the protozoa from the liver cyst that will fill the palm of your hand). If these abscesses rupture, the contents will be described as **anchovy paste**—dark brown. You do NOT need to drain these liver abscesses (almost every abscess needs surgical drainage). Diagnosis involves identifying trophozoite forms in stool. Trophozoites have **4 nuclei** and may **contain ingested red blood cells**. Treat with metronidazole (acute illness) and iodoquinol (cyst carriers). Be cautious: Echinococcus, a helminth, which also starts with "E," causes liver abscesses you DO need to drain/remove, while *Entamoeba histolytica*, a protozoan, which starts with "E," causes liver abscesses that you DON'T need to drain/remove. *Yersinia enterocolitica* is a bacterium that causes bloody diarrhea.

Giardia lamblia causes **fatty, foul-smelling diarrhea** (steatorrhea) on **camping trips**. It is transmitted fecal-oral, and for the test, almost always involves a hiking trip in which the patient drinks from a stream or lake (fresh water) without treating the water first. Cysts are in contaminated water, human drinks water, trophozoites form in the gut. It is a **pear-shaped** organism with a **pair of nuclei,** a **suction disk**, and four pairs of flagella. That disk adheres to the mucosal surface of the small intestine, physically blocking the absorption of nutrients, particularly of fat. This causes foul-smelling, fatty, **osmotic diarrhea** (steatorrhea—if you haven't studied diarrhea or GI yet, we are repeating steatorrhea on purpose). *Giardia* can be diagnosed with **stool antigen detection** or visualization of organisms. Treat this with metronidazole.



(a) (b) (c)

Figure 1.2: *Giardia* and *Cryptosporidium*
(a) High-power magnification of *Giardia* cysts. (b) High-powered magnification of multiple *Cryptosporidium* trophozoites. They are pear-shaped and multiply flagellated, and contain dual nuclei. (c) Low-powered view of an acid-fast stain of stool showing *Cryptosporidium* cysts, staining red.

Cryptosporidium parvum causes **watery diarrhea in AIDS**. *Crypto* causes a **self-limiting watery diarrhea** in immunocompetent patients; treatment is rarely needed. In immunocompromised patients it can cause massive fluid loss, warranting intravenous fluid replacement. Treatment does not involve giving antiparasitic medications; keeping the patient hydrated and preventing further inoculation by **straining water** is all that is needed. This organism does a little changeup with its life cycle, but don't get tricked. **Oocysts** are the reproductive cell, so they are not cyst cysts. In the process of keeping it simple, consider *Cryptosporidium* to follow the same model as the previous two. Cysts in the water get ingested and become the active trophozoite in the gut. Trophozoites make cysts that are shed in the stool. It just happens that in *Cryptosporidium*, the cyst is called an oocyst. We are not going to cover the mechanism of oocyst formation or reproduction in *Cryptosporidium* because that process is outside a human and does not directly cause disease. Don't learn it. Unlearn it if you know it (unless you plan on doing Trop Med).

Urogenital Protozoa

There is only one of these you need to know. It is *Trichomonas vaginalis*, a sexually transmitted infection.

***Trichomonas vaginalis*.** "Trich" has **no cyst form**. Because it has no cyst form, because it exists only as a trophozoite, it cannot exist outside of humans. Inoculation is through sexual contact. It is one of three classic vulvovaginitis infections, trich presenting with **watery greenish vaginal discharge** and foul-smelling odor, with itching, burning, or pain of the vagina. Physical exam will show a strawberry cervix. It is generally asymptomatic in men, who act as carriers. If you treat only one partner, she will be reinfected by the still-infected partner. If he gets treated, but not she, she will reinfect him. This trading infection after cure back and forth is termed "ping-ponging." Both partners must be treated at the same time, and then, as long as they are monogamous, no more disease. It is diagnosed by simple inspection on a **wet mount** which reveals a pear-shaped organism, a central nucleus, and **four anterior**

flagella. The other causes of vulvovaginitis are bacterial, which do not move. Finding **motile organisms** on a wet mount of vaginal secretions is a freebie—*Trichomonas vaginalis*. And they move; they are described as "zipping" because they move so fast (the four flagella). Treatment is metronidazole for **both symptomatic partner and asymptomatic partner**. One more time for super emphasis—the "both partners" part was bolded and not the drug name.

Protozoa Transmitted by Insects, Not Malaria

Those that infect the blood and visceral organs are not ingested but are instead carried by a vector that inoculates the human through a bite. There is a common theme throughout this class of protozoa. Because they are carried by a vector, they do not need a cyst form. They do have two forms, though. The motile, flagellated protozoan form will be carried in an insect vector. The flagellated form gets into a human because of the bug bite. The motile, flagellated form will be seen on blood smear during an acute infection. The motile flagellated form swims to its preferred tissue. When the flagellated form gets to its target tissue it transforms into the nonflagellated. The nonflagellated form generally causes disease. The concept of flagellated in human blood, nonflagellated in human tissue is the key. What vector carries the flagellated form, and which tissue the flagellated form targets for disease, vary by organism.

Trypanosoma cruzi. Carried in the **reduviid bug** vector (also called the triatomine bug and the kissing bug), *Trypanosoma cruzi* is the South American *Trypanosoma* that causes South American disease. The bug and the disease it causes are not nearly as deadly as the African species (discussed next). The **flagellated** form is called a trypomastigote and the **nonflagellated** form is called an amastigote. The flagellated version of this protozoan is in the reduviid bug's feces. The bug bites a human. The flagellated form in the bug feces gets into the human wound. Inside the human it swims in the bloodstream and gets to cardiac tissue and neurons of the gut. Memorize it, don't try to make sense of it. Those are the places *T. cruzi* goes. There, it becomes the nonflagellated form which results in **Chagas disease**. Chagas disease is caused by the nonflagellated amastigote's eating up of neurons and myocytes. In the esophagus, the loss of the myenteric plexus leads to achalasia (megaesophagus). In the colon, the loss of the myenteric plexus causes megacolon. The myenteric plexus is needed for gut motility. Where the protozoa live, neurons die, and that segment of the GI tract loses peristalsis. These guys also get into myocytes, where they cause myocarditis and heart block.

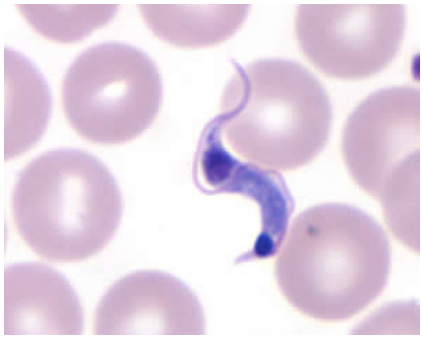
Acute vs. chronic disease, Chagas. Every text and review resource loves to cite the **Romaña sign**, a unilateral periorbital swelling associated with contamination of the eye by the bug's feces. It is more of a sign that a person has been near a reduviid bug, than a sign of acute Chagas disease. Many sources imply that Chagas disease is an acute illness; that the megacolon, megaesophagus, or heart failure from myocarditis occurs in patients after they return from endemic areas. While **acute Chagas disease** can result in CHF from myocarditis, most cases of acute disease are completely asymptomatic. **Chronic Chagas disease**, decades after being infected, is where we find the megacolon, megaesophagus, and heart block. The patient suffers symptoms decades after exposure to the bug. During the workup, a biopsy is done for the symptom or finding. No one thinks, "*based on this history and physical, you have Chagas disease; let's confirm my suspicion by getting a biopsy.*" Instead, the reasoning goes, "*Well this sure is a mystery, I wonder what is UP with your esophagus!? We should get a biopsy. WHOA! Chagas disease! I remember that from medical school! I will write this up and present it at a national conference.*" Treatment is with benznidazole or nifurtimox.

However, if you see a question where there is information regarding RECENT travel to South America, this diagnosis should remain on your list. From a test-taking standpoint, South America + mega-GI = *T. cruzi* Chagas.

You may have noticed that the nonflagellated form doesn't make flagellated versions or go back to flagellated versions in our story. The story goes this way so you remember the key to making the

diagnosis of all vector-borne protozoa—acute disease is diagnosed with a blood smear showing flagellated organisms, chronic disease is diagnosed with tissue biopsy. One more time.

Acute, blood smear, trypomastigotes with flagella; chronic, tissue biopsy, amastigotes without flagella.



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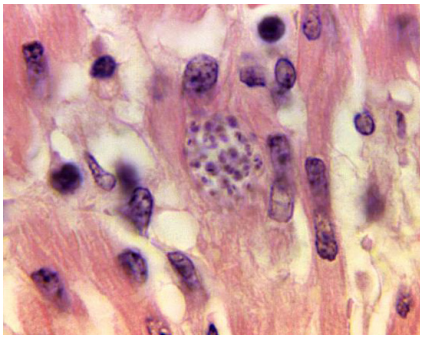

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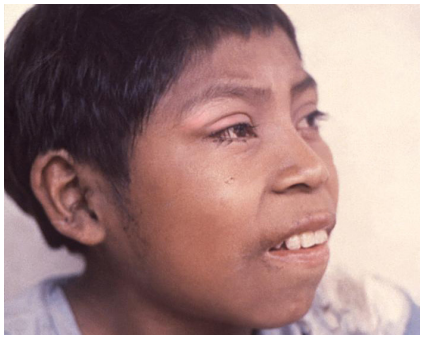


(c)

Figure 1.3: *Trypanosoma cruzi*
(a) A blood smear depicting the dark blue flagellated trypomastigotes, indicating the acute form of the disease. (b) Nonflagellated forms in clusters within cardiac muscle. The streaks of red are muscle; the dark blue circles are the amastigote. (c) The Romaña sign, lid swelling.

***Trypanosoma brucei*.** The African form of *Trypanosoma* causes **African sleeping sickness**. The flagellated form is carried by an insect vector (the **tsetse fly**); the target organ is brain neurons. When the flagellated form gets to brain neurons, it becomes the nonflagellated form in brain neurons. The acute phase is characterized by an **ulcer at the bite site**, a **cyclic fever** about every 2 weeks, and posterior cervical lymph node enlargement. The disease is a **progressive demyelinating encephalitis**. This is a slow process. At first, headache. Over weeks, progressive somnolence predominates, and weakness is felt. Over months the disease progresses to confusion, coma, and eventual death. Look for the flagellated forms on **blood smear**. Blood smear is chosen for practical reasons. Brain biopsies are not common in sub-Saharan Africa, nor are neurosurgeons in general. Getting a brain biopsy would show the nonflagellated organisms and is the diagnostic method of choice for chronic disease. It's just more practical to stick someone's vein and look with microscope than cut open their head and take a piece of brain. Treat with **suramin** before the encephalitis develops. Melarsoprol if it is in the CNS.

***Leishmania donovani*.** Leishmaniasis is primarily an African and Brazilian disease—that history of travel to the endemic area must be included for you to suspect the disease. The flagellated form of the protozoan (called a promastigote) is transmitted by an insect vector (the **sandfly**). The flagellated form is seen on blood smear during acute disease. Acute disease could be **visceral leishmaniasis** that affects the reticuloendothelial system (which is the spleen and bone marrow), presenting with hepato**splenomegaly**, pancytopenia, and fevers. Acute disease could also be **cutaneous leishmaniasis** which causes skin ulcers. Treat with sodium stibogluconate.

Protozoa Transmitted by Insects, Malaria

***Plasmodium* species** cause **malaria** in Africa. This is a disease you should know well because we know so much about it. You must be provided the history of travel to Africa to consider malaria. But if you have that information? Get ready. There is much to know.

The definitive host is within the **anopheles mosquito**. The anopheles mosquito is also the vector, how humans get inoculated with *Plasmodium*. The life cycle in humans is very complicated, with difficult-to-pronounce words. We're going to do this without the malaria words first, then do it again in the next paragraph inserting malaria vocabulary. A mosquito bites a human, inoculating the bloodstream

with *Plasmodium*. The liver cells, hepatocytes, take up the *Plasmodium*. Within the hepatocyte, the *Plasmodium* multiplies. No good for hepatocyte, which pops when too full of *Plasmodium*. This spills a shit ton of *Plasmodium* into the blood. *Plasmodium* actually doesn't like hepatocytes very much. *Plasmodium* loves red blood cells. Most of the *Plasmodium* does the same thing to red blood cells as it did to the hepatocyte. They get into the cell, replicate, and pop the red blood cell, dumping a shit ton of *Plasmodium* into the blood to go infect more red blood cells. But every once in a while, some of the *Plasmodium* decide they are going to make gametes. When the mosquito comes back around for another meal, slurp slurp slurpin' it up, the mosquito ingests the gametocytes. In the mosquito, sexual maturation. It is outside the human and does not cause disease. Do not learn it.

Now with malaria words. A mosquito bites a human carrying **sporozoites** (*Plasmodium* released from an oocyst). The sporozoites get taken up into the hepatocyte. Sporozoites cannot infect red blood cells. The sporozoite folds itself into a ball, and is termed a **trophozoite.** That cell undergoes massive nuclear division, forming thousands of nuclei. This one-cell-with-thousands-of-nuclei is called a **schizont.** A cell membrane forms between all the nuclei, making thousands of single-nucleus cells called **merozoites.** The hepatocyte pops, releasing merozoites into the bloodstream. Merozoites infect red blood cells. When they infect a red blood cell they curl into a ball and become red blood cell **trophozoites**. This merozoite-derived trophozoite does to the red blood cell what the sporozoite-derived trophozoite did to the hepatocyte: form a schizont that becomes a bunch of merozoites. Red blood cell pops, merozoites are released, go infect more red blood cells. But every once in a while that immature trophozoite develops into **gametocytes** (*Plasmodium* in the sexual cycle in the mosquito) which are eaten by the mosquito. In the mosquito those gametocytes do some stuff you don't have to know but result in the oocyst's rupture and the release of sporozoites.

There are four kinds of *Plasmodium*. *P. vivax* and *P. ovale* form **hypnozoites** that remain latent in the liver for years, causing relapses in treated individuals. *P. falciparum* and *P. malariae* do not form hypnozoites.

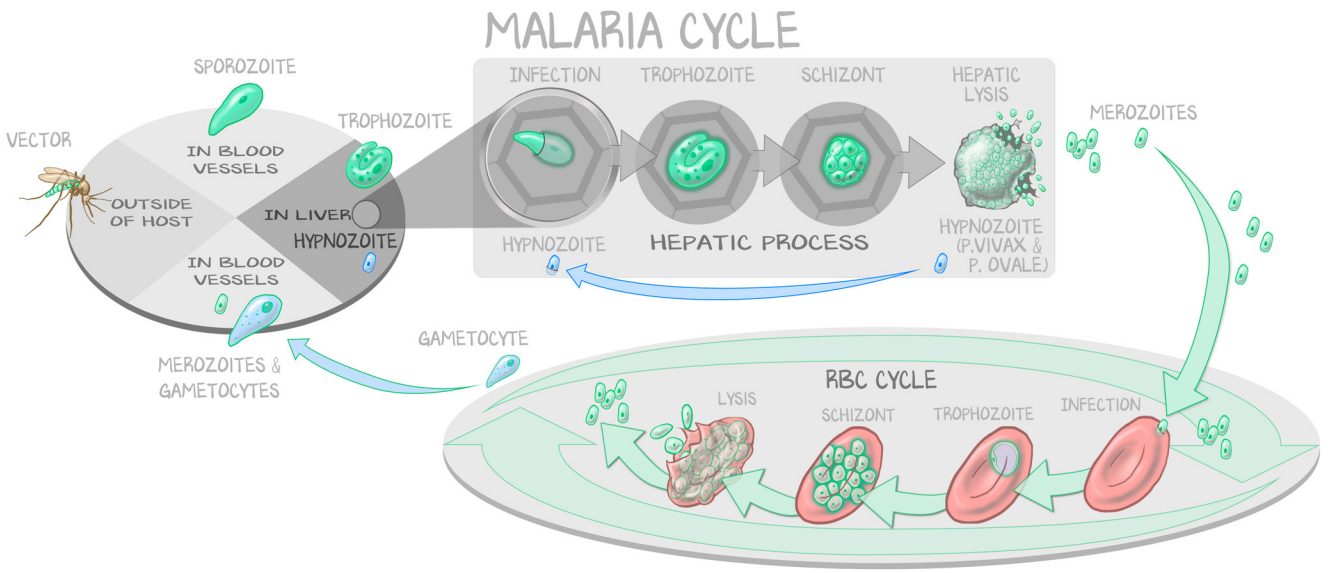


Figure 1.4: Malaria Life Cycle and Vocabulary
Follow left to right along the top, the from right to left along the bottom. An Anopheles mosquito bites a human, injecting the sporozoite into the bloodstream. It swims to the liver where it infects a hepatocyte and becomes a trophozoite. The trophozoite divides its nucleus many times to become a schizont. The schizont fills the cell, drops membranes to form individual protozoa, then pops the hepatocyte, releasing tons of merozoites into the bloodstream. Merozoites are like the sporozoites, except they love RBCs. Merozoites infect RBCs, turn into ringed trophozoites, multiply into a schizont, then pop the RBCs, releasing more merozoites. The cycle of merozoites-RBCs-merozoites continues. Every once in a while, a gametocyte is released from an RBC instead. Gametocytes don't do anything in humans except float through the bloodstream until an Anopheles mosquito takes a blood meal. Into the mosquito it goes, outside-of-human-protozoan magic . . . now there are sporozoites in the Anopheles mosquito to be given to another human host.

Sporozoite	Comes from mosquito; infects hepatocytes.
Trophozoite	The curled-up ring form of *Plasmodium*. Sporozoites curl into a trophozoite in hepatocytes; merozoites curl into trophozoites in RBCs.
Schizont	The big bag of nuclei that will become merozoites. The trophozoite divides nuclei to become schizonts. When those nuclei get their own plasma membrane, they become merozoites.
Merozoite	What comes out of infected cells and what infects RBCs. Sporozoites become schizonts in hepatocytes, and exit as merozoites in blood. Merozoites become schizonts in RBCs, and exit as more merozoites in blood.
Hypnozoite	Sneaky merozoite that reinfects hepatocytes and stays dormant. *P. vivax* and *P. ovale* only.
Gametocyte	Merozoites come out of RBCs to infect more RBCs. Sometimes, some become gametocytes to be taken up by the mosquito.

Table 1.2: Translating Malaria into English

Malaria is a **cyclic febrile disease**. Fevers occur because the schizont ruptures and organisms are released into the bloodstream. That takes time to happen. When they infect another red blood cell, when they are out of plasma and hidden from the immune system, the symptoms go away. In the RBC (out of plasma) the merozoites go through the cycle again, schizont to merozoite, popping the RBC when finished with it. When the red blood cell pops, organisms are back in the blood and symptoms recur. Organisms in the blood cause **fever, chills,** and **sweating**. *P. malariae* is cyclical every 72 hours; the others are cyclical every 48 hours. Malaria causes **splenomegaly** as it sequesters infected red blood cells. The spleen lyses infected cells, and the malaria lyses infected cells, both producing a **hemolytic anemia**.

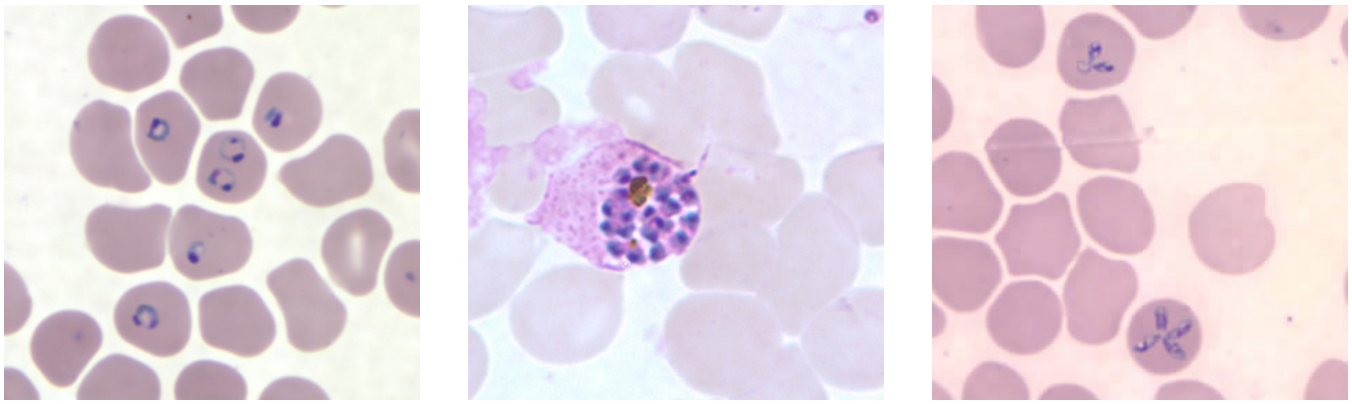
Sickle cell trait (heterozygous for the sickle β-globin gene) is protective against malaria, which is why sickle cell disease is so prevalent in Africa and amongst African Americans in the US. Sickle cell disease (homozygous for sickle β-globin) would be more protective against malaria if it weren't a fatal disease without substantial medical intervention. African children with sickle cell disease generally do not survive to adulthood. Sickle cell trait does not induce sickling except in the most severe conditions, such as climbing Mount Everest without an oxygen tank (which would kill anyone, even without sickle cell trait). Because the trait confers survival benefit against malaria and doesn't cause any of the morbidity or mortality of sickle cell disease, the prevalence of the allele has increased substantially in populations stressed by malaria. Because malaria is an African disease, sickle cell trait and sickle cell disease are problems for African Americans.

P. vivax and *P. ovale* form hypnozoites; they can cause relapse after treatment.
P. malaria cycles at 72 hours.
P. falciparum **f**---s you up. The infected RBCs occlude capillaries everywhere, leading to death of the organs.

The diagnosis is made on a **thick and thin blood smear**. On the thick and thin blood smear (not just a look at blood on a slide—you must request a thick and thin smear), you will see either red blood cells with **ring-shaped trophozoites** within them OR the **red blood cell replaced by nuclei**, the schizont. You should be able to immediately identify the blood smear as malaria. If you are given blood smear, the answer is contained within the smear.

Prophylaxis you should know. Treatment is only for score augmentation beyond 250. If you as the prescriber know **for sure** the patient is traveling to regions where the endemic malaria is already **confirmed to be chloroquine sensitive**, use chloroquine prophylaxis. If you don't know for certain the endemic malaria is chloroquine sensitive, use mefloquine. They both are -quines.

Treatment is as complicated as its life cycle. You do need to know treatment if you are looking for a 250+ (opposed to other treatments in this lesson which get you that 270). All *Plasmodium* is treated with **chloroquine** if susceptible. If resistant to chloroquine, use **mefloquine** or **atovaquone-proguanil**. For life-threatening infections, use **intravenous quinidine**. If there are liver hypnozoites, **add primaquine**. When traveling to endemic areas, chloroquine was recommended, but with increases in resistance, prophylaxis is with **mefloquine**, which is continued for four weeks after you return.



(a) (b) (c)

Figure 1.5: Malaria and *Babesia*
(a) A blood smear showing RBCs with ringed trophozoites. This is a sample from *Plasmodium malariae*. Without context, this could represent any *Plasmodium* species or even *Babesia*. (b) A blood smear with a schizont, the red blood cell swollen with dark purple nuclei. All *Plasmodium* species and *Babesia* form schizonts before exiting the RBC. (c) A blood smear showing the Maltese cross of babesiosis.

Babesia*.** Babesiosis is "malaria" of the US. It follows a very similar pattern, is a disease that happens in the US, and is often tested against malaria. Its vector is the ***Ixodes tick (the same vector that carries *Borrelia burgdorferi* that causes Lyme disease), and is found in the northeastern US. Lyme disease is named for the towns in Connecticut where the disease was first characterized as an epidemic (Lyme, Old Lyme, East Lyme). While the *Ixodes* tick, Lyme disease, and babesiosis can be found sporadically throughout the United States, the endemic area remains the northeast. On a vignette, there is no reason to name the state in the question stem unless the location is THE KEY CLUE and contains the answer. The *Babesia* get into red blood cells, replicate within, then pop. There is **fever**, chills, and sweats. The spleen identifies them as infected, captures them (**splenomegaly**) and lyses them (hemolytic **anemia**). The *Babesia* lyse the red blood cells (more hemolytic anemia). The *Babesia* reproduce within red blood cells, causing **almost cyclic fevers** (they vary between 48-72 hours), splenomegaly, and anemia (just like malaria symptoms). What you should know about them is how to spot them on the blood smear. The blood smear always contains the key clue, better than any state. The red blood smear will show the **ring-shaped trophozoites** ("the same" as malaria) or the **tetrads** resembling the **Maltese cross.** Be able to recognize the Maltese cross in red blood cells. Nothing else in human disease does that (Figure 1.6c).

Others

These last two are clinically significant, are not diagnosed by a blood smear, go between the cyst and oocyst form (similar to the cyst and trophozoite form), and, because they have no overlap with others, are given their own final section.

***Toxoplasma gondii*.** This tissue protozoan is ingested but is not an intestinal parasite, nor is it transmitted by an insect vector. There are three ways to get *Toxoplasma* as a human—eating cat poop, eating raw meat infected with *Toxoplasma*, or being a fetus whose mother gets *Toxoplasma* in one of the

previous two ways. Inactive *Toxoplasma* exists in animal vectors such as sheep, pigs, and mice. If humans eat **undercooked** meat, and that meat has inactive *Toxoplasma* **cysts**, *Toxoplasma* gets into humans. It activates (comes out of the cyst) in the gut, oocysts are shed in the stool, AND **tissue cysts form**. If a cat eats raw meat, and that meat has inactive *Toxoplasma* cysts, *Toxoplasma* gets into cat. But cat doesn't have to worry. *Toxoplasma* activates in cat's gut where it IS an intestinal parasite. Cat then poops out active *Toxoplasma* (oocyst). Humans clean the litter box of said cat, and microscopic oocysts are ingested. Oocyst gets into human, and tissue cysts form. Either way, **humans get tissue cysts.**

Cat eats the tissue cysts and poops out oocysts, which other animals eat, and get tissue cysts for the cat to eat again (the cat's prey). Cats are spared disease. Human eats the tissue cysts (undercooked lamb or pork), and then tissue cysts form in human (**ingestion** transmission). Humans are near cat feces that have oocysts (**cat feces** transmission is also ingestion). If mom is pregnant and gets infected through ingestion of undercooked meat OR cat feces, *Toxo* is given to fetus (**transplacental** transmission). After one exposure, as long as you don't get AIDS, you are then immune to *Toxoplasma*. It is the woman who is antibody-negative (never exposed) who cleans litter boxes and is exposed to *Toxo* for the first time who messes up baby.

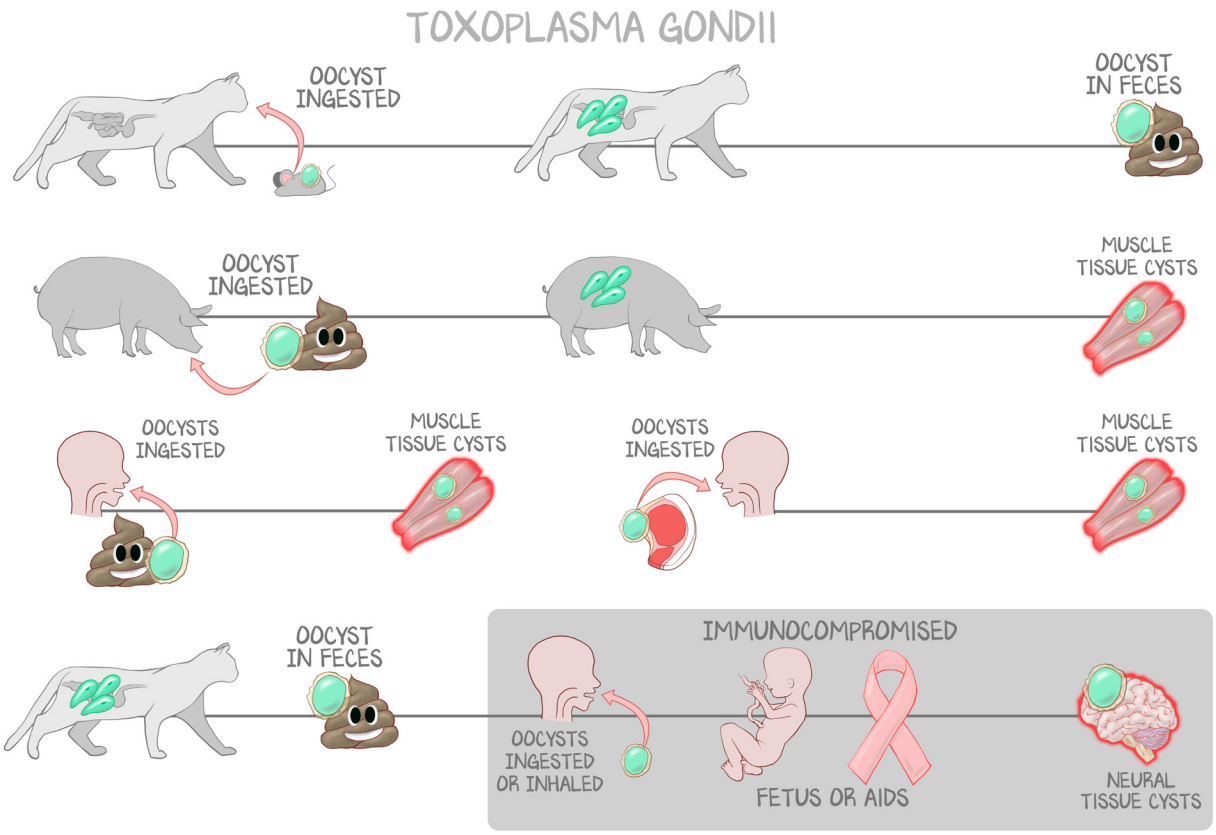


Figure 1.6: *Toxoplasma gondii*
Toxo likes the gut of cats. If cats eat oocysts, oocysted Toxo (the same as encysted Toxo for our purposes) turns into the trophozoite form, which reproduces and lays more oocysts. Toxo doesn't like any other organism's gut. When another animal eats oocysts, Toxo excysts to a larvae, leaves the gut through the bloodstream, and goes into tissue (specifically skeletal muscle), and encysts, where it waits for a cat to eat the animal. Humans count as "other animals." So, if a human eats meat with encysted Toxo in it (which excysts into a larva in the human gut) OR if a human eats the oocysts pooped by a cat (which mature into larvae in the human gut), the human will get tissue cysts. But only immunocompromised humans (AIDS, the fetus of a mother without immunity to Toxo) suffer cysts. The worst form of Toxo cysts in humans is in the brain.

Immunocompetent humans laugh in the face of *Toxoplasma*, and do NOT develop cysts. Textbooks say, *"mono-like reaction,"* but really that means, "*some viral bleh, I felt awful one time, was it the flu? I don't know, I didn't get tested because it lasted only 2 days.*" Oh, and bee tee dub, you are now immune. I know this because you have a positive *Toxoplasma* IgG antibody. IgG antibodies are good. Immunocompromised patients, specifically those with **AIDS**, develop **ring-enhancing lesions** in the **brain**. In immunocompromised hosts, such as the **developing fetus,** you get intracranial calcifications, chorioretinitis, and hydrocephalus. Treatment is with **pyrimethamine and sulfadiazine**.

***Naegleria fowleri*.** This is super diddily duper rare. It crawls in through your nose while you are swimming in freshwater ponds, penetrates the CNS via the cribriform plate, and is highly fatal. It is highly fatal, but scantly infectious. But! If you see **amoebas in CSF**, it is *Naegleria fowleri*.

IF YOU SEE	GET A	LOOK FOR	MEANS
Bloody diarrhea and liver abscess	Stool	Red blood cells ingested in trophozoite	*Entamoeba histolytica*
Steatorrhea and hiking or camping	Stool	Pear-shaped, multiple flagella	*Giardia lamblia*
Watery diarrhea and AIDS patient	Stool	Acid-fast stain	*Cryptosporidium*
Itching, burning, discharge from vagina	Wet mount	Four flagella, leaf-shaped	*Trichinella*
Achalasia, megacolon, or heart block, South America	Tissue	Nonflagellated organism inside tissue cells	Chagas disease, *T. cruzi*
Progressive somnolence to coma	Blood smear	Flagellated organism outside RBC	*T. brucei*
HSM, anemia, Africa	Blood smear	Flagellated organism outside RBC	*Leishmania*
Cyclical fevers, Africa, HSM, anemia	Blood smear	Ring trophozoites and mature schizont	Malaria
Cyclical fevers, US, HSM, anemia	Blood smear	Ring trophozoites and Maltese cross	*Babesia*
Ring-enhancing lesions and AIDS	IgM	Positive against *Toxoplasma*	Toxoplasmosis
A young kid quickly dying after swimming in a lake	CSF	Amoebas	*Naegleria*

Table 1.3: Rapid Recall for Protozoa

VECTOR	PROTOZOAN	DISEASE
Tsetse fly	*T. brucei*	African sleeping sickness
Anopheles mosquito	*Plasmodium malariae*	Malaria
Ixodes tick	*Babesia*	Babesiosis
Reduviid bug/kissing bug	*T. cruzi*	Chagas disease
Sandfly	*Leishmania*	Leishmaniasis
Cat feces	*Toxoplasma gondii*	Ring-enhancing lesions/AIDS Birth defects fetus

Table 1.4: Vector and Protozoan

BUG	ASSOCIATIONS
Entamoeba histolytica	Bloody diarrhea and liver abscesses Flask-shaped abscesses on biopsies of colon Trophozoites have four nuclei and ingest red blood cells Liver cysts, anchovy paste, do not need to drain Metronidazole or iodoquinol
Giardia lamblia	Steatorrhea/malabsorption diarrhea = fatty diarrhea Camping or hiking trips, drinking fresh water Pear-shaped trophozoite, pair of nuclei, flagella Suction disk adheres to the intestinal mucosa, physical barrier for absorption Metronidazole
Cryptosporidium	Watery diarrhea in AIDS patient Oocyst on acid-fast stain of the stool Filter water

Table 1.5: Intestinal Protozoa

BUG	ASSOCIATIONS
T. cruzi	Reduviid bug vector in Central/South America Acute disease = flagella on blood smear (almost never actually symptomatic) Chronic disease = no flagella on tissue biopsy, biopsy the organ of Chagas disease Chagas disease = megacolon, megaesophagus, myocarditis ← decades after exposure Albendazole
T. brucei	Tsetse fly in Africa Ulcer at bite site Months of progressive demyelinating encephalitis, African sleeping sickness Suramin
Leishmania donovani	Sandfly vector in Africa Reticuloendothelial system = hepatosplenomegaly, pancytopenia Cutaneous = ulcers Stibogluconate or Ampho B
Plasmodium species	Anopheles mosquito vector in Africa Sporozoites infect liver, curl into trophozoites, replicate nuclei to form schizont; Schizont forms membrane between individual nuclei to make merozoites; Merozoites rupture RBC, swim in blood, infect other RBCs, curl into trophozoites, repeat Fevers, shaking, chills every 48 hours *P. vivax* and *P. ovale* form hypnozoites; they can cause relapse after treatment *P. malaria* cycles at 72 hours *P. falciparum* **f**---s you up = thrombosis of small arteries, multiorgan failure Thick and thin smear shows trophozoites or schizonts in RBCs Chloroquine if known to be susceptible endemically Mefloquine or atovaquone/proguanil if not Severe cases are given intravenous quinidine
Babesia	*Ixodes* vector (same as Lyme disease), northeastern United States The US form of malaria Fever, hemolytic anemia, splenomegaly, and not-so-cyclical 48–72 hours variably Thick and thin Maltese cross in RBCs Atovaquone and azithromycin

Table 1.6: Insect Vector Protozoa

BUG	ASSOCIATIONS
Trichomonas vaginalis	No cyst form, only lives in humans Traded between partners, treat both (ping-ponging) Four anterior flagella, single nucleus, pear-shaped Motile on wet mount Odor, green discharge from vagina, itching, burning Metronidazole
Toxoplasma gondii	AIDS patients get ring-enhancing lesions on CT Pregnant mothers get their fetus intracranial calcifications, hydrocephalus, chorioretinitis Human eating undercooked meat with cysts gives human cyst disease Human ingesting cat feces with oocysts gives human cyst disease Humans who get cyst disease and have a fetus give fetus cyst disease Pyrimethamine and sulfadiazine
Naegleria fowleri	Freshwater lakes, swimming Enter cribriform plate Rapidly fatal brain infection (meningitis-encephalitis) Amoebas in CSF Amphotericin

Figure 1.7: The Other Protozoa